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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	10/051,452	ZON ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on April 29, 2004 has been entered. The claims pending in this application are claims 1-9 and 12. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn.

Specification

2. The substitute specification filed on April 29, 2004 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because applicant does not provide the substitute specification in a clean form (without markings). Since the substitute specification has not been entered, the following objection is maintained.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 14, line 10). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

3. Claim 1 is objected to because of the following informality: "construct" should be "constructs".

4. Claim 3 is objected to because of the following informality: "HA" is an abbreviation. It can only be used after this phrase appears once.

Response to Arguments

In page 6, last paragraph of applicant's remarks, applicant argues that "[A]pplicants note that HA and FLAG epitopes are not abbreviations, or, are commonly listed commercially by these names".

This argument has been fully considered and the examiner has partially withdrawn the objection on claim 3 in view of the amendment filed on April 29, 2004. However, it is not persuasive toward the withdrawal of the objection on "HA" since this is known that HA is an abbreviation and represents influenza A virus haemagglutinin.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 is rejected as vague and indefinite because it is unclear that "pooled plasmid clones" in step d) mean plasmid clones or mean bacterial clones having a plasmids. Please clarify.

8. Claim 5 is rejected as vague and indefinite in view of the phrase "cDNA constructs having specific protein motifs that have been selected by polymerase chain reaction" because it is unclear that the polymerase chain reaction in this phrase is a method step or not. If the

polymerase chain reaction is a method step, it is unclear that this step is before or after step a). Please clarify.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 2, 4, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, (Cell, 68, 775-785, 1992) in view of Sugano *et al.*, (Gene, 120, 227-233, 1992).

Lin *al.*, teach expression cloning of TGF-β type II receptor, a functional transmembrane serine/threonine kinase.

Regarding claims 1 and 2, since Lin *et al.*, teach to prepare a cDNA library using E. Coli strain MC106/P3, culture $5x10^3$ to 10^4 recombinant bacteria on Luria broth agar Petri dishes containing ampicillin and tetracycline, scrap bacteria colonies from the dishes and isolate

plasmid DNAs from the bacteria colonies (see page 783, left column), Lin *et al.,* disclose preparing a cDNA library comprising bacterial cells comprising more than one cDNA plasmid constructs wherein the constructs are contained in bacteria cells, culturing the bacterial cells of step a) to produce clones wherein each clone corresponds to a single tagged cDNA construct, arraying the individual bacterial clones, pooling a predetermined number of arrayed clones (ie., blue colonies on the plate) and isolating plasmid DNA from them, thereby producing pooled plasmids as recited in steps a) to d) of claim 1. Since Lin *et al.,* teach to transfect each pool of plasmid cDNA into a mammalian cell line (ie., COS-M6 cell), measure the binding of the transfected cells to [^{125}I]TGF-β1, and repeat above transfection and binding assays for several rounds until a single positive clone that can bind to [^{125}I]TGF-β1 has been identified (see page 783, left column), Lin *et al.,* disclose transfecting suitable mammalian host cells with pooled plasmids and assaying the expressed polypeptides for a biochemical activity of interest as recited in steps e) and f) of claim 1, and repeating steps d) through f) one or more times and thereby identifying a cDNA construct encoding the polypeptide having the biochemical activity of interest (ie., binding to [^{125}I]TGF-β1) as recited in step g) of claim 1 wherein steps d) through f) are repeated until a single cDNA construct expressing a polypeptide having the biochemical activity of interest is identified as recited in claim 2.

Regarding claim 4, Lin *et al.,* teach: i) obtaining double-stranded CDNA from cells expressing a polypeptide with the biochemical activity of interest (ie., binding to [^{125}I]TGF-β1); ii) ligating the cDNA into a vector; and iii) transforming competent bacterial cells with the cDNA construct of step ii) (see page 783, left column).

Regarding claim 8, since that the binding of the transfected cells to [^{125}I]TGF-β1 is by protein-protein interaction, claim 8 is anticipated by Lin *et al.,*

Lin *et al.,* do not disclose to a tagged cDNA expression library as recited in claim 1, 2, and 4.

Sugano *et al.,* teach use of an epitope-tagged cDNA library to isolate cDNA encoding proteins with nuclear localization potential using tag specific antibody wherein the expression vector in the epitope-tagged cDNA library comprises a coding region for a tag (ie., 85-aa N-terminal peptide of the SV40 T antigen) operably linked to a promoter (ie., EF204 promoter) (see abstract in page 227 and page 228).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used a tagged cDNA expression library to perform the method recited in claims 1, 2, 4, and 8 wherein the expression vector in the epitope-tagged cDNA library comprises a coding region for a tag (ie., 85-aa N-terminal peptide of the SV40 T antigen) operably linked to a promoter (ie., EF204 promoter) in view of prior art of Lin *et al.,* and Sugano *et al.*. One having ordinary skill in the art would have been motivated to do so because Sugano *et al.,* has successfully used an epitope-tagged cDNA library to isolate cDNA encoding proteins with nuclear localization potential and the replacement of a cDNA library (ie., a cDNA library taught by Lin *et al.,*) by another cDNA library (ie., an epitope-tagged cDNA library taught by Sugano *et al.,*) in order to perform the method recited in claims 1, 2, 4, and 8 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the epitope-tagged cDNA library taught by Sugano *et al.,* would be used to identify new gene products with

an unknown function whose properties can be assayed using antibodies against the tagged epitope (see page 227, right column and page 228, left column).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above, and further in view of Dymecki (US 2002/0170076 A1, filed on May 30, 1997).

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra*.

Lin *et al.*, and Sugano *et al.*, do not disclose that the tagged cDNA plasmid constructs comprise a tag that is selected from the group consisting of: Glutathione S-Transferase (GST-), c-Myc (Myc-), HA-, FLAG epitope (FLAG-) and poly-Histidine (His-) as recited in claim 3.

Dymecki teaches that useful peptide tag-binder pairs such as GST-glutathione, polyHis-divalent metal, 9E10 Myc epitope-antibody, and SV40 T antigen-antibody are exchangeable (see column 6, [0049]).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used a tagged plasmid comprising GST or poly-

histidine to prepare a tagged cDNA expression library recited in claim 3 in view of prior art of Lin *et al.*, Sugano *et al.*, and Dymecki. One having ordinary skill in the art would have been motivated to do so because a plasmid comprising GST or poly-histidine is commercially available and the simple replacement of one kind of plasmid (i.e., a tagged plasmid comprising SV40 T antigen taught by Sugano *et al.*,) from another kind of plasmid (i.e., tagged plasmid comprising GST or poly-histidine taught by Dymecki) during the process of preparing a tagged cDNA expression library recited in claim 3 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

12. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above, or claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above, and further in view of Goodearl *et al.*, (US Patent NO. 5,530,109, published on June 25, 1996).

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra.*

In view of ambiguity of claim 5 (see above rejection on claim 5 under 35 USC 112, second paragraph), if claim 5 is read as that the tagged cDNA library comprises cDNA constructs having specific protein motifs that can be selected by polymerase chain reaction, TGF-β type II receptor in the library taught by Lin *et al.*, can be amplified by polymerase chain reaction. Therefore, claim 5 is being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above.

Alternatively, if polymerase chain reaction recited in claim 5 is a method step, another rejection is made as following.

Lin *et al.*, and Sugano *et al.*, do not disclose that the tagged cDNA library comprises cDNA constructs having specific protein motifs that are selected by polymerase chain reaction as recited in claim 5.

Goodearl *et al.*, teach to amplify coding fragment for a specific gene from a cDNA library by PCR (see column 40, example 10).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have amplified coding fragment for a specific gene (ie., having specific protein motifs) from a cDNA library by PCR in view of prior art of Lin *et al.*, Sugano *et al.*, and Goodearl *et al.*. One having ordinary skill in the art would have been motivated to do so because PCR would provide a simple and excellent way to amplify coding fragment for a specific gene (ie., having specific protein motifs) from a cDNA library (see Goodearl *et al.*, column 40, example 10). One having ordinary skill in the art at the time the

invention was made would have been a reasonable expectation of success to amplify coding fragment for a specific gene (ie., having specific protein motifs) from a cDNA library.

13. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4 and 8 above, and further in view of Wilson *et al.*, (US Patent No. 5,932,211, filed on November 28, 1994).

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra.*

Lin *et al.*, and Sugano *et al.*, do not disclose to use an EF-1α promoter in the expression vector recited in claim 6.

Wilson *et al.*, teach that chimeric rIDS cDNA is operably linked to human EF-1 promoter (see column 18, first paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used human EF-1 promoter as a promoter in the expression vector recited in claim 4 in view of prior art of Lin *et al.*, Sugano *et al.*, and Wilson *et al.*. One having ordinary skill in the art would have been motivated to do so because the simple replacement of one kind of promoter with known properties (i.e., EF204 promoter taught by Lin *et al.*,) from another kind of promoter with known properties (i.e., EF-1 promoter taught by Wilson *et al.*,) during the process of constructing an expression vector recited in claim 4 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

14. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above, and further in view of Adamou *et al.*, (US Patent No. 5,811,535, filed on August 1996).

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra.*

Lin *et al.*, and Sugano *et al.*, do not disclose that the mammalian host cells used in step e) are 293 T fibroblast cells as recited in claim 7.

Adamou *et al.*, teach that a mammalian cell used for the transfection is COS or 293 cells wherein COS and 293 cells are exchangeable (see column 28, lines 39-65).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used 293 T fibroblast cells as recited in claim 7 to perform the method as recited in claim 1 in view of prior art of Lin *et al.*, Sugano *et al.*, and Adamou *et al.*. One having ordinary skill in the art would have been motivated to do so because the simple replacement of one cell line with known properties (i.e., COS cells taught by Lin *et al.*,) from another cell line with known properties (i.e., 293 cells taught by Adamou *et al.*,) during the process of performing the method as recited in claim 7 would have been, in the

absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the method step recited in claim 1.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.6, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

15. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above.

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra.* Lin *et al.*, teach that each pool of clones comprises $5x10^3$ to 10^4 recombinant bacteria (see page 783, left column).

Lin *et al.*, and Sugano *et al.*, do not disclose that each pool of clones comprises from about 2 to about 1000 clones as recited in claim 9.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 9 wherein each pool of clones comprises from about 2 to about 1000 clones in view of prior art of Lin *et al.*, and Sugano *et al.*... One having ordinary skill in the art has been motivated to do so because

optimization of clone number of each pool of bacterial clones during the process of performing the method recited in claim 9, in the absence of convincing evidence to the contrary, would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to optimize clone number of each pool of bacterial clones. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

16. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, in view of Sugano *et al.*, as applied to claims 1, 2, 4, and 8 above, and further in view of Short (US Patent No. 6,057,103, filed on August 26, 1997).

The teachings of Lin *et al.*, and Sugano *et al.*, have been summarized previously, *supra.*

Lin *et al.*, and Sugano *et al.*, do not disclose more than one expression libraries wherein each expression library comprises a different cell type which is stimulated with a specific stimulus as recited in claim 12.

Short teaches gene libraries generated from one or more uncultured microorganisms. This allows one to access untapped resources of biodiversity (see column 5). Since uncultured

microorganisms are environmental samples, the environments that the microorganisms are exposed to are considered as specific stimuli as recited in claim 12.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made more than one expression libraries wherein each expression library comprises a different cell type which is stimulated with a specific stimulus in view of prior art of Lin *et al.*, Sugano *et al.*, and Short. One having ordinary skill in the art would have been motivated to do so because Short suggests that construction of more than one gene libraries would allow one to access untapped resources of biodiversity (see column 5). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make more than one expression libraries wherein each expression library comprises a different cell type which is stimulated with a specific stimulus.

Conclusion

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is 571-272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
August 2, 2004

FRANK LU
PATENT EXAMINER